



# The evaluation of carotid intima thickness in clinical and subclinical hypothyroidism and effects of thyroid hormone treatment

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**Abstract:** Objectives: In this study, our aim was to investigate the CA-IMT in clinical hypothyroidism(CH) and subclinical hypothyroidism(SCH) and the effects of L-thyroxine replacement. Materials and methods: The study group consisted of 20 patients with clinical hypothyroidism(CH group) and 20 patients with subclinical hypothyroidism(SCH group) and 20 patients with normal thyroid hormone function tests (control group). Serum TSH, fasting glucose, lipid profile(total cholesterol, HDL-cholesterol, LDL-cholesterol, and triglyceride),HbA1c,insulin,HOMA and carotid intima media thickness(CA-IMT) of all subjects were measured at admission. Thereafter, all hypothyroid patients received L-thyroxine treatment. The previous tests were re-examined after achievement of euthyroidism for 6 months. The results of the tests before and after L- thyroxine treatment were compared. Results: The levels of TSH, total cholesterol, triglyceride, LDL for CH and SCH group were statistically different before and after treatment( $p \leq 0.05$ ). The levels of glucose, HDL,VLDL, HbA1c, insulin and HOMA for CH and SCH group were similar before and after treatment( $p \geq 0.05$ ). The difference of CA-IMT for both sides before and after treatment was statistically significant( $p \leq 0.05$ ). Conclusion: This study suggests that subjects with clinical and subclinical hypothyroidism are characterized by an increment in the CA-IMT resulting from an adverse lipid profile, which can be reversed by thyroid hormone replacement. So, thyroid hormone replacement may be helpful to prevent or at least slow down atherosclerosis in hypothyroid subjects.

**Keywords:** Hypothyroidism, L- thyroxine, CA-IMT

## 1. Introduction

With the improvement of laboratory techniques, thyroid gland diseases has become more prevalent. Depending on the levels of thyroid hormones,it may present either as normo- hypo-hyperthyroidism. It can also be classified as subclinical(normal thyroid stimulating hormone-TSH) or clinical(abnormal TSH). Subclinical hypothyroidism(SCH) is the most common form.

Cardiovascular diseases are the main causes of death in the world. The comorbidity of atherosclerosis with various diseases has garnered attention in recent years. Carotid intima media thickness(CA-IMT) measurement by Doppler Ultrasonography(USG) is a validated method to determine

extent of atherosclerosis[1,2]. Age, male sex, smoking, diabetes, hypertension, dyslipidemia, obesity, sedentary lifestyle,high hs-CRP, homocysteine, lipoprotein, and plasminogen activator inhibitor 1 (PAI-1) are among the well-known risk factors for atherosclerosis[3]. In this study, our aim was to investigate the CA-IMT in clinical hypothyroidism(CH) and subclinical hypothyroidism(SCH) and the effects of L-thyroxine replacement.

## 2. Materials and Methods

### 2.1. Study Population

The study group consisted of 20 patients with clinical hypothyroidism(CH group) and 20 patients with subclinical

hypothyroidism(SCH group) and 20 patients with with normal thyroid hormone function tests(control group). Inclusion criterias were to be aged between 18 and 65 years, to have thyroid hormone dysfunction assessed by laboratoryfindings, to have a bodymass index(BMI) of 20–30 kg/m<sup>2</sup> and not to be on thyroid hormone replacement. Exclusion criterias were to have history of diabetes mellitus,hypertension,coronary artery disease,renal failure,malignant disease,liver diseases and familial hypercholesterolemia, to be using lipid lowering drugs, to have BMI<20 kg/m<sup>2</sup> or>30 kg/m<sup>2</sup> and smoking. The study protocol was approved by local ethics committees and informed consent was obtained from each patient. The study was performed according to the recommendations of the Declaration of Helsinki.

## 2.2. Study Design

Demographical,clinical and laboratory findings were recorded for each subject after a standard examination including detailed medical history; measurement of fasting glucose,lipid profile(total cholesterol,HDL cholesterol,LDL cholesterol and triglyceride) and measurementof blood pressure,height and weight. Also, the risk of atherosclerosis was assessed by the measurement of CA-IMT.

Thereafter, all hypothyroid patients received L-thyroxine treatment. Patients were re-evaluated every four weeks based on TSH and fT<sub>4</sub> levels to adjust the dose. The dose that achieved a normal serum TSHwas subsequently maintained. After a normal TSH level was obtained, patients were seen every four weeks to assess the presence of adverse effects, disease progression and whether the L-thyroxine dose needed adjustment.

Normalization of serum TSH levels required about approximately 7.2 ±5.4and 9.8 ±4.8 months in patients with subclinical and clinical hypothyroidism, respectively. The previous tests werere-examined after achievement of euthyroidism for 6 months.

## 2.3. Laboratory Measurements

Serum TSH, fT<sub>3</sub> and fT<sub>4</sub> were measured by chemiluminescence method by an automated analyzer (Immulite2000, Siemens, Germany). Normal ranges for fT<sub>3</sub> were1.8–4.6 pg/mL, for fT<sub>4</sub> 0.93–1.7 ng/dL and for TSH 0.27–4.2mU/mL.

## 2.4. Measurement of CA-IMT

Ultrasonographic studies on common carotid arteries were carried out by gray-scale highresolutioncolor Doppler ultrasound(Siemens,Germany) equipped with 13MHz lineartransducer. To avoid interobserver variability, all measurements were performed by the same examiner who was blinded to the subjects clinical status. The examiner performed all procedures on both sides of two longitudinal

images of the each common carotid artery on the morning in supine position. Average of the two CA-IMT(proximal and distal) values from eachside was used to calculate mean CA-IMT on each side.

## 2.5. Statistical Analysis

The SPSS statistical software package(SPSS, version 10.0 for Windows; SPSS Inc, Chicago, IL) was used to perform all statistical calculations. Adequacy of all parameters to normal distribution was tested by using Kolmogorov-Smirnov test. Comparison of the groups were done by using 'one way ANOVA'. Differences were considered statistically significant at  $p \leq 0.05$ .

# 3. Results

The study group consisted of 20 patients with clinical hypothyroidism(CH group),20 patients with subclinical hypothyroidism(SCH group) and 20 subjects with normal thyroid hormone function tests (control group).

## 3.1. Demographic Properties

In all groups; 5(25%) of the subjects were males,15(75%) of the subjects were females. The age,weight, height, BMI of the subjects in all three groups are summarized in Table 1. The groups were similar in terms of age and sex( $p \geq 0.05$ ).

**Table 1.** The demographic properties and personal variables of the subjects

	Age	Height	Weight	BMI
CH group	37.65±1.27	164.78±1.89	73.90±2.29	27.87±1.89
SCHgroup	34.47±1.43	165.64±1.66	68.45±1.78	28.42±1.86
Control group	35.25±2.21	165.20±1.81	70.38±3.92	27.97±4.15

## 3.2. Laboratory Measurements

Serum TSH, fasting glucose, lipid profile(total cholesterol, HDL cholesterol,LDL cholesterol and triglyceride), HbA1c, insulin, HOMA of all subjects were measured at admission. Thereafter all hypothyroid patients received L thyroxine treatment. Normalization of serum TSH levels required about approximately 7.2 ±5.4and 9.8 ±4.8 months in patients with subclinical and clinical hypothyroidism. The previous tests were re-examined after achievement of euthyroidism for 6 months. The results of the tests before and after L-thyroxine treatment are summarized in Table 2.

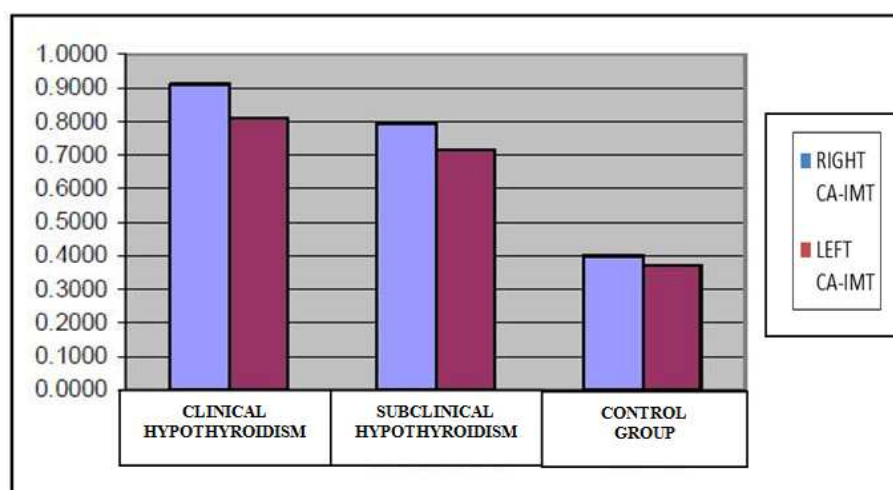
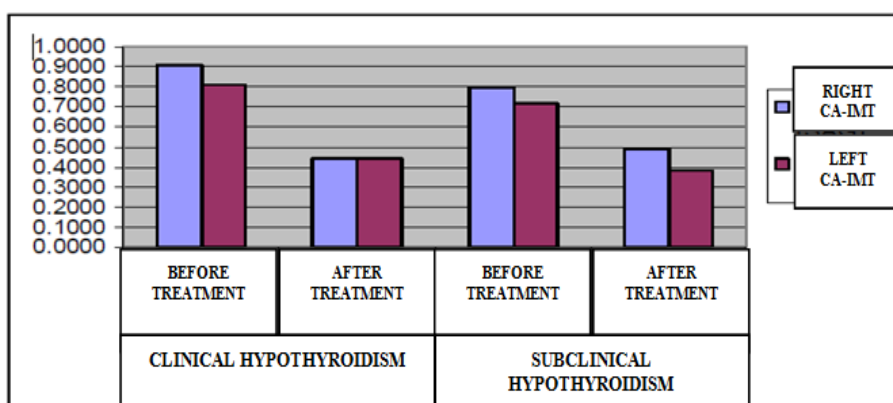
*Table 2. The laboratory measurements before and after L-thyroxine treatment*

	CH GROUP			SCH GROUP			CONTROL GROUP
	BEFORE TREATMENT	AFTER TREATMENT	P	BEFORE TREATMENT	AFTERTREATMENT	p	
<b>TSH</b>	117.8±5.25	7.75±1.11	≤0.05	8.97±1.1	2.94±0.43	≤0.05	3.50±0.43
<b>Glucose</b>	91.05±6.4	91.35±7.4	≥0.05	92.50±9.3	91.40±7.9	≥0.05	95.00±8.5
<b>Total Cholesterol</b>	216.30±6.2	167.80±9.7	≤0.05	192.55±11.2	138.600±9.5	≤0.05	120.00±9.4
<b>Triglyceride</b>	135.30±7.9	110.45±6.9	≤0.05	139.40±7.8	105.20±7.6	≤0.05	105.00±10.3
<b>HDL</b>	54.65±6.89	49.65±4.12	≥0.05	49.45±4.7	47.90±4.3	≥0.05	45.00±5.3
<b>LDL</b>	127.75±8.8	93.40±8.7	≥0.05	104.05±9.45	82.10±6.4	≥0.05	90.00±5.8
<b>VLDL</b>	26.33±4.78	24.90±2.45	≥0.05	26.45±3.34	25.60±2.4	≥0.05	25.00±3.6
<b>HbA1c</b>	5.51±1.15	5.42±1.1	≥0.05	5.38±1.1	5.48±1.5	≥0.05	5.50±1.1
<b>Insulin</b>	8.94±1.34	9.11±2.1	≥0.05	8.93±1.5	9.54±1.2	≥0.05	8.00±1.7
<b>HOMA</b>	2.12±0.12	2.11±0.43	≥0.05	2.04±0.5	2.16±0.2	≥0.05	1.87±0.32

The levels of TSH, total cholesterol, triglyceride, LDL for CH and SCH group were statistically different before and after treatment ( $p \leq 0.05$ ). The levels of glucose, HDL, VLDL, HbA1c, insulin and HOMA for CH and SCH group were similar before and after treatment ( $p \geq 0.05$ ).

Before treatment, the right CA-IMT of CH group, SCH group and control group were  $0.91 \pm 1.61$ ,  $0.78 \pm 0.40$ ,  $0.40 \pm 1.23$ . Before treatment, the left CA-IMT of CH group, SCH group and control group were  $0.81 \pm 0.93$ ,  $0.70 \pm 0.85$ ,  $0.37 \pm 0.21$  respectively. The CA-IMT of both right and left sides for CH group, SCH group and control group was different before treatment ( $p \leq 0.05$ ).

### 3.3. Measurement of CA-IMT

*Figure 1. The evaluation CA-IMT of CH group, SCH group and control group before treatment**Figure 2. The evaluation CA-IMT of CH group and SCH group before and after treatment*

After treatment, the right CA-IMT of CH group and SCH group were  $0.44 \pm 0.36$ ,  $0.48 \pm 0.41$ . After treatment, the left CA-IMT of CH group and SCH group were  $0.44 \pm 0.12$ ,  $0.38 \pm 0.23$ . The difference of CA-IMT for both sides before and after treatment was statistically significant ( $p \leq 0.05$ ).

## 4. Discussion

It is controversial whether hypothyroidism results in increased risks of cardiovascular disease and whether thyroid hormone replacement reverses or prevents these risks. The findings of the current study showed a significant difference in the CA-IMT at baseline between euthyroid controls and patients with clinical and subclinical hypothyroidism despite subclinical state and after achieving euthyroidism for 1 year; the CA-IMT in patients with clinical and subclinical hypothyroidism decreased to that of euthyroid controls. Clinical and subclinical hypothyroidism resulted in an early atherosclerotic change in the vascular wall and thyroid hormone replacement reversed this change. A decrement in LDL-cholesterol after thyroid hormone replacement was independently associated with regression of the increased CA-IMT.

Many studies have examined the relationship between clinical and subclinical hypothyroidism and cardiovascular diseases. However, some studies reported subclinical hypothyroidism to increase cardiovascular risk[4-6] and others studies showed no such effect[7-9]. Recently, well-controlled studies have documented a relationship between subclinical hypothyroidism and a reversible atherosclerotic vascular lesion. Monzani *et al.*[10] and Nagasakiet *al.*[11] reported that patients with subclinical hypothyroidism have a higher CA-IMT and increased brachial-ankle pulse wave velocity, a useful indicator of arterial stiffness and that thyroid hormone replacement regress CA-IMT and decrease brachial-ankle pulse wave velocity.

This study suggested that the altered lipid metabolism was a major mechanism leading to early atherosclerotic vascular changes in clinical and subclinical hypothyroidism. Indeed, other mechanisms may be involved in the pathogenesis of atherosclerotic vascular alterations resulting from hypothyroidism. Recently, it has been reported that Hashimoto's thyroiditis results in low-grade chronic inflammation which causes endothelial dysfunction, a promoter of atherosclerosis[12,13]. Also chronic activation of the immune system due to Hashimoto's thyroiditis is considered an alternative mechanism for inducing atherosclerosis[14], but the mechanism is not well-elucidated.

There were some limitations in the present study. The number of subjects participating in this study was small and the design was not placebo-controlled. Although the CA-IMT is an important forecaster for atherosclerotic cardiovascular diseases, we did not observe more direct cardiovascular events and mortality.

Therefore, a long-term study will be needed to investigate the effect and mechanism of clinical and

subclinical hypothyroidism on atherosclerosis or cardiovascular diseases and the benefit of thyroid hormone replacement in clinical and subclinical hypothyroidism.

In conclusion, our study suggests that patients with clinical and subclinical hypothyroidism are characterized by an increment in the CA-IMT resulting from an adverse lipid profile, which can be reversed by thyroid hormone replacement.

Therefore, thyroid hormone replacement may be helpful to prevent or at least slow down atherosclerosis in hypothyroid subjects.

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There are no conflicts of interest for all authors.

## References

- [1] O'Leary DH, Polak JF. Intima-media thickness: a tool for atherosclerosis imaging and event prediction. *American Journal of Cardiology* 2002;90:18-21.
- [2] Baldassarre D, Tremoli E, Amato M, Veglia F, Bondioli A, Sirtori CR. Reproducibility validation study comparing analog and digital imaging technologies for the measurement of intima-media thickness. *Stroke* 2000;31:1104-1110.
- [3] P. M. Ridker PM, M. J. Stampfer MJ, and N. Rifai N. Novel risk factors for systemic atherosclerosis: a comparison of C-reactive protein, fibrinogen, homocysteine, lipoprotein(a), and standard cholesterol screening as predictors of peripheral arterial disease. *JAMA* 2001;285: 2481-2485.
- [4] Razvi S, Shakoob A, Vanderpump M, Weaver JU, Pearce SH. The influence of age on the relationship between subclinical hypothyroidism and ischemic heart disease: a metaanalysis. *J Clin Endocrinol Metab* 2008;93: 2998-3007.
- [5] Hak AE, Pols HA, Visser TJ, Drexhage HA, Hofman A, Witteman JC. Subclinical hypothyroidism is an independent risk factor for atherosclerosis and myocardial infarction in elderly women: the Rotterdam Study. *Ann Intern Med* 2000;132: 270-278.
- [6] Walsh JP, Bremner AP, Bulsara MK, O'Leary P, Leedman PJ, Feddema P, Michelangeli V. Subclinical thyroid dysfunction as a risk factor for cardiovascular disease. *Arch Intern Med* 2005;165: 2467-2472.
- [7] Kuller LH, Burke GL, Tracy RP, Ladenson PW. Thyroid status, cardiovascular risk, and mortality in older adults. *JAMA* 2006;295: 1033-1041.
- [8] Rodondi N, Newman AB, Vittinghoff E, de Rekeneire N, Satterfield S, Harris TB, Bauer DC. Subclinical hypothyroidism and the risk of heart failure, other cardiovascular events, and death. *Arch Intern Med* 2005;165: 2460-2466.
- [9] Chiche F, Jublanc C, Coudert M, Carreau V, Kahn JF, Bruckert E. Hypothyroidism is not associated with increased carotid atherosclerosis when cardiovascular risk factors are accounted for in hyperlipidemic patients. *Atherosclerosis* 2008;203: 269-276.

- [10] Bots ML, Hoes AW, Koudstaal PJ, Hofman A, Grobbee DE. Common carotid intima-media thickness and risk of stroke and myocardial infarction: the Rotterdam Study. *Circulation* 1997; 96: 1432-1437.
- [11] Nagasaki T, Inaba M, Henmi Y, Kumeda Y, Ueda M, Tahara H, Sugiguchi S, Fujiwara S, Emoto M, Ishimura E, Onoda N, Ishikawa T, Nishizawa Y. Decrease in carotid intima-media thickness in hypothyroid patients after normalization of thyroid function. *Clin Endocrinol (Oxf)* 2003; 59: 607-612.
- [12] Taddei S, Caraccio N, Virdis A, Dardano A, Versari D, Ghiadoni L, Ferrannini E, Salvetti A, Monzani F. Low-grade systemic inflammation causes endothelial dysfunction in patients with Hashimoto's thyroiditis. *J Clin Endocrinol Metab* 2006;91: 5076-5082.
- [13] Kvetny J, Heldgaard PE, Bladbjerg EM, Gram J. Subclinical hypothyroidism is associated with a lowgrade inflammation, increased triglyceride levels and predicts cardiovascular disease in males below 50 years. *Clin Endocrinol (Oxf)* 2004; 61: 232-238.
- [14] Xiang GD, He YS, Zhao LS, Hou J, Yue L, Xiang HJ. Impairment of endothelium-dependent arterial dilation in Hashimoto's thyroiditis patients with euthyroidism. *Clin Endocrinol (Oxf)* 2006;64: 698-702.